

WHAT IS CLAIMED IS:

1. A method for prolonging the *in vivo* effect of Type I interferon (IFN), comprising:

administering to a patient in need of Type I IFN therapy a complex of Type I IFN and a subunit of the human interferon α/β receptor (IFNAR) which is capable of binding to the Type I IFN of the complex, in an amount effective to provide such IFN therapy.

wherein said Type I IFN has a sequence consisting essentially of the sequence of

- a) a native Type I IFN;
- b) a fragment of a) which has Type I IFN biological activity;
- c) a variant of a) or b) which has at least 70% sequence identity with a) or b) and which has Type IFN biological activity;
- d) a variant of a) or b) which is encoded by a DNA sequence which hybridizes to the complement of the native DNA sequence encoding a) or b) under moderately stringent conditions and which has Type I IFN biological activity; or
- e) a salt or functional derivative of a), b), c), or d) which has Type I IFN biological activity; and

wherein said IFNAR has a sequence consisting essentially of the sequence of

- f) a native human IFNAR polypeptide chain;
- g) a fragment of f) which has IFNAR biological activity;

h) a variant of f) or g) which has at least 70% sequence identity with f) or g) and which has IFNAR biological activity;

i) a variant of f) or g) which is encoded by a DNA sequence which hybridizes to the complement of the native DNA sequence encoding f) or g) under moderately stringent conditions and which has IFNAR biological activity; or

j) a salt or functional derivative of f), g), h), or i) which has IFNAR biological activity.

2. A method in accordance with claim 1, wherein said complex comprises a non-covalent complex of said Type I IFN and said IFNAR.

3. A method in accordance with claim 2, wherein said Type I IFN and said IFNAR are administered separately and said complex is formed *in vivo*.

4. A method in accordance with claim 1, wherein said complex comprises a complex in which said Type I IFN is bound to said IFNAR by a covalent bond.

5. A method in accordance with claim 1, wherein said complex comprises a fusion protein in which said Type I IFN is bound to said IFNAR by a peptide bond.

6. A method in accordance with claim 5, wherein said Type 1 IFN is linked to said IFNAR by means of a peptide linker.

7. A method in accordance with claim 1, wherein said Type I IFN is an IFN α , an IFN β , or an IFN ω .

8. A method in accordance with claim 7, wherein said Type I IFN is IFN β .

9. A method in accordance with claim 1, wherein said IFNAR is the beta subunit of the human interferon α/β receptor (IFNAR2).

Sub B1
10. A molecule comprising a complex of a Type I interferon (IFN) and a subunit of the human interferon α/β receptor (IFNAR) which is capable of binding to the Type I IFN of the complex, in which said Type I IFN is bound to said IFNAR by a covalent bond or a peptide bond,

wherein said Type I IFN has a sequence consisting essentially of the sequence of

- a) a native Type I IFN;
 - b) a fragment of a) which has Type I IFN biological activity;
 - c) a variant of a) or b) which has at least 70% sequence identity with a) or b) and which has Type I IFN biological activity;
 - d) a variant of a) or b) which is encoded by a DNA sequence which hybridizes to the ~~complement~~^{complement} of the native DNA sequence encoding a) or b) under moderately stringent conditions and which has Type I IFN biological activity; or
 - e) a salt or functional derivative of a), b), c), or d) which has Type I IFN biological activity; and
- wherein said IFNAR has a sequence consisting essentially of the sequence of
- f) a native human IFNAR polypeptide chain;

g) a fragment of f) which has IFNAR biological activity;

h) a variant of f) or g) which has at least 70% sequence identity with a) or b) and which has IFNAR biological activity;

i) a variant of f) or g) which is encoded by a DNA sequence which hybridizes to the ^{complement}complement of the native DNA sequence encoding f) or g) under moderately stringent conditions and which has IFNAR biological activity; or

j) a salt or functional derivative of f), g), h), or i) which has IFNAR biological activity.

14 ~~11~~. A molecule in accordance with claim ~~10~~¹³, wherein said Type I IFN is bound to said IFNAR by a covalent bond.

15 ~~12~~. A molecule in accordance with claim ~~10~~¹³, wherein said Type I IFN is bound to said IFNAR by a peptide bond.

16 ~~13~~. A molecule in accordance with claim ~~12~~¹⁵, wherein said Type 1 IFN is linked to said IFNAR by means of a peptide linker.

17 ~~14~~. A molecule in accordance with claim ~~13~~¹⁶, wherein said peptide linker is (GGGGS)_n ^(SEQ ID NO: 1) wherein n=1-5.

18 ~~15~~. A molecule in accordance with claim ~~10~~¹³, wherein said Type I IFN is an IFN α , an IFN β , or an IFN ω .

19 ~~16~~. A molecule in accordance with claim ~~15~~¹⁸, wherein said Type I IFN is IFN β .

20 ~~17~~. A molecule in accordance with claim ~~10~~¹³, wherein said IFNAR is the beta subunit of the human interferon α/β receptor (IFNAR2).

22 ~~18~~. A DNA encoding a fusion protein which is a molecule in accordance with claim ~~12~~¹⁵.

23 ~~19~~. A host cell transformed with a vector carrying a DNA in accordance with claim ~~18~~²² in a manner which permits expression of said fusion protein.

24 ~~20~~. A method of making a fusion protein comprising culturing a host cell in accordance with claim ~~19~~²³ and recovering the fusion protein expressed thereby.

25 ~~21~~. A method for improving the shelf life of Type I interferon, comprising storing said interferon in the form of a complex in accordance with claim 10 or a complex in which said IFN is bound to said IFNAR by a non-covalent bond.

Sub 3
22. A pharmaceutical composition ^{consisting essentially of} comprising a pharmaceutically acceptable carrier and a complex of a Type I interferon (IFN) and a subunit of the human interferon α/β receptor (IFNAR) which is capable of binding to the Type I IFN of the complex,

wherein said Type I IFN has a sequence consisting essentially of the sequence of

a) a native Type I IFN;
B b) a fragment of a) which has Type I IFN biological activity;

c) a variant of a) or b) which has at least 70% sequence identity with a) or b) and which has Type I IFN biological ^{agonist} activity;

d) a variant of a) or b) which is encoded by a DNA sequence which hybridizes to the ^{complement} of the native DNA

sequence encoding a) or b) under moderately stringent

conditions and which has Type I IFN biological activity; or

e) a salt or functional derivative of a), b), c), or

d) which has Type I IFN biological activity; and

wherein said IFNAR has a sequence consisting essentially of the sequence of

f) a native human IFNAR polypeptide chain;

g) a fragment of f) which has IFNAR biological activity;

h) a variant of f) or g) which has at least 70% sequence identity with f) or g) and which has IFNAR biological activity;

i) a variant of f) or g) which is encoded by a DNA sequence which hybridizes to the complement of the native DNA sequence encoding f) or g) under moderately stringent conditions and which has IFNAR biological activity; or

j) a salt or functional derivative of f), g), h), or

i) which has IFNAR biological activity.

23. A method for potentiating the biological effects of Type I interferon (IFN), comprising:

administering to a patient in need of Type I IFN therapy a subunit of the human interferon α/β receptor (IFNAR) which is capable of binding to the native Type I IFN to be potentiated, in an amount effective to provide such IFN therapy potentiating effects,

wherein said IFNAR has a sequence consisting essentially of the sequence of

- a) a native human IFNAR polypeptide chain;
- b) a fragment of a) which has IFNAR biological activity;
- c) a variant of a) or b) which has at least 70% sequence identity with a) or b) and which has IFNAR biological activity;
- d) a variant of a) or b) which is encoded by a DNA sequence which hybridizes to the ^{complement} ~~complement~~ of the native DNA sequence encoding a) or b) under moderately stringent conditions and which has IFNAR biological activity; or
- e) a salt or functional derivative of a), b), c), or d) which has IFNAR biological activity.

SECRET